

CLAIM AMENDMENTS

This listing of claims will replace all prior versions, and listings, of claims in the application.

1.-2. (Canceled)

3. (Currently amended) A method according to any one of claims 27, 28, 29, 30, 33, 34, 35, 52, 53, 54, or 61, 55 or 56, wherein said ~~first and second~~ greater than 50 different oligonucleotides are labeled.

4. (Currently amended) A method according to claim 3, wherein said ~~first and second~~ greater than 50 different oligonucleotides bear different labels.

5.-6. (Canceled)

7. (Currently amended) A method according to any one of claims 27, 29, 30, 33, 34, 35, 52, 53, or 54, 55 or 56, wherein said first substrate comprises discrete sites to which said ~~first and second~~ greater than 50 different oligonucleotides are covalently ~~may be~~ linked.

8.-9. (Canceled)

10. (Currently amended) The method according to claim 9 27, 33, 35, 54, or 61, wherein said ~~first and second~~ greater than 50 different oligonucleotides are synthesized by a synthesis method selected from the group consisting of printing and photolithography.

Claims 11-26 (canceled)

27. (Currently amended) A method for multiplex detection of target nucleic acids comprising:

a) providing a first substrate comprising ~~at least first and second~~ greater than 50 different oligonucleotides linked to said first substrate through ~~first and second~~ cleavable linkers, respectively, said ~~first and second~~ greater than 50 different oligonucleotides having sequences different from each other, wherein said substrate comprises an array of discrete sites to which said greater than 50 different oligonucleotides are covalently linked;

b) cleaving said ~~first and second~~ linkers, thereby releasing said ~~first and second~~ greater than 50 different oligonucleotides from said substrate thereby generating a pool of oligonucleotides comprising said greater than 50 different oligonucleotides ~~said first and second oligonucleotides~~;

c) contacting said ~~first and second~~ pool of oligonucleotides with a composition comprising ~~at least a first and second~~ different target nucleic acids, whereby said ~~first and second~~ different target nucleic acids hybridize with said ~~first and second~~ greater than 50 different oligonucleotides in said pool of oligonucleotides;

d) modifying said ~~first and second~~ greater than 50 different oligonucleotides in said pool of oligonucleotides hybridized with said ~~first and second~~ different target nucleic acids to produce modified ~~first and second~~ oligonucleotides, and

e) contacting said modified ~~first and second~~ oligonucleotides with a second substrate comprising ~~at least first and second~~ probe oligonucleotides, said ~~first and second~~ probe oligonucleotides having sequences different from each other and having sequences different from said ~~first and second~~ greater than 50 different oligonucleotides released from said first substrate, whereby said target nucleic acids are detected.

28.-32. (Canceled)

33. (Currently amended) A method for multiplex detection of target nucleic acids comprising:

a) providing a first substrate comprising ~~at least first and second~~ greater than 50 different oligonucleotides covalently linked to said first substrate through ~~first and second~~ cleavable linkers, ~~respectively~~, said ~~first and second~~ greater than 50 different oligonucleotides having sequences different from each other, wherein said first substrate comprises an array of discrete sites to which said great than 50 different oligonucleotides are covalently linked;

b) cleaving said ~~first and second~~ linkers, thereby releasing said greater than 50 different ~~first and second~~ oligonucleotides from said first substrate thereby generating a pool of oligonucleotides comprising said greater than 50 different ~~said first and second~~ oligonucleotides;

c) contacting said ~~first and second~~ pool of oligonucleotides with a ~~first and second~~ different target nucleic acids;

d) modifying said ~~first and second~~ greater than 50 different oligonucleotides in said pool of oligonucleotides contacted with said ~~first and second~~ different target nucleic acids to produce modified ~~first and second~~ modified oligonucleotides;

e) contacting said modified ~~first and second~~ oligonucleotides with a second substrate comprising ~~at least first and second~~ probe oligonucleotides, said ~~first and second~~ probe oligonucleotides having sequences different from each other and having sequences different from said ~~first and second~~ pool of oligonucleotides released from said substrate, and

f) detecting said target nucleic acids.

34. (Canceled)

35. (Currently amended) A method for multiplex detection of target nucleic acids comprising:

a) cleaving ~~at least first and second~~ greater than 50 different oligonucleotides linked to a first substrate through at least a first cleavable linker from said first substrate, wherein said first substrate comprises an array of discrete sites to which said greater than 50 different oligonucleotides are covalently linked, thereby releasing said ~~first and second~~ greater than 50 different oligonucleotides from said first substrate generating a pool of oligonucleotides comprising said ~~first and second~~ oligonucleotides, said ~~first and second~~ greater than 50 different oligonucleotides having sequences different from each other; and

b) contacting said ~~first and second~~ pool of oligonucleotides with a ~~first and second~~ different target nucleic acids;

c) modifying said ~~first and second~~ greater than 50 different oligonucleotides contacted with said ~~first and second~~ different target nucleic acids to produce modified ~~first and second~~ oligonucleotides, and

d) contacting said modified ~~first and second~~ oligonucleotides with a second substrate comprising ~~at least first and second~~ probe oligonucleotides, said ~~first and second~~ probe oligonucleotides having sequences different from each other and having sequences different from said ~~first and second~~ greater than 50 different oligonucleotides released cleaved from said first substrate, and

d) detecting said target nucleic acids.

36. (Currently amended) The method according to claim 27, 33, 34 or 35, 54 or 61, wherein said first substrate is selected from the group consisting of glass, plastics, polysaccharides, nylon, nitrocellulose resins, silica, silicon, carbon, and metals.

37. (Currently amended) The method according to claim 27 29, wherein said first and second substrates comprises a chip.

Claims 38.-53 (canceled)

54. (Currently amended) A method for multiplex detection of target nucleic acids comprising:

a) providing a first substrate comprising ~~at least first and second~~ greater than 50 different oligonucleotides linked to said first substrate through ~~first and second~~ cleavable linkers, ~~respectively~~, said ~~first and second~~ greater than 50 different oligonucleotides having different sequences, wherein said first substrate comprises an array of discrete sites to which said greater than 50 different oligonucleotides are covalently linked;

b) cleaving said ~~first and second~~ linkers, thereby releasing said ~~first and second~~ greater than 50 different oligonucleotides from said substrate thereby generating a pool of oligonucleotides comprising said ~~first and second~~ greater than 50 different oligonucleotides;

c) contacting said ~~first and second~~ pool of oligonucleotides with a composition comprising ~~at least a first and second~~ different target nucleic acids, whereby said ~~first and second~~ target nucleic acids hybridize with said ~~first and second~~ greater than 50 different oligonucleotides in said pool of oligonucleotides;

d) modifying said ~~first and second~~ greater than 50 different oligonucleotides hybridized with said ~~first and second~~ target nucleic acids to produce modified ~~first and second~~ oligonucleotides[[,]]; and

e) contacting said modified ~~first and second~~ oligonucleotides with a second substrate comprising ~~at least first and second~~ probe oligonucleotides, said ~~first and second~~ probe oligonucleotides having sequences being different from each other and having sequences different from said ~~first and second~~ greater than 50 different oligonucleotides released from said first substrate, said ~~first and second~~ probe oligonucleotides being distributed randomly on said second substrate, whereby said target nucleic acids are detected.

55.-56. (Canceled)

57. (Currently amended) A method according to claim 27, 33, ~~28, 29,30, 34~~, 35, 54 or 61, ~~55 or 56~~, wherein said modifying step comprises sequencing or amplification.

58. (Currently amended) A method according to claim 27, ~~28, 29,30~~, 33, 34, 35, 54 or 61, ~~55 or 56~~, wherein said modifying step comprises ~~an assay selected from~~ polymerase chain reaction (PCR), ~~ligase chain reaction (LCR), cycling probe technology (CPT), Invader,~~ oligonucleotide ligation assay (OLA) and single base extension (SBE).

59.-60. (Canceled)

61. (New) A method for multiplex detection of target nucleic acids comprising:

- a) providing a first substrate on which are disposed different beads having greater than 50 different oligonucleotides covalently linked to said different beads through cleavable linkers, said greater than 50 different oligonucleotides having sequences different from each other, wherein said first substrate comprises an array of discrete sites on which said beads are disposed;
- b) cleaving said linkers, thereby releasing said greater than 50 different oligonucleotides from said beads, thereby generating a pool of oligonucleotides comprising said greater than 50 different oligonucleotides;
- c) contacting said pool of oligonucleotides with different target nucleic acids;
- d) modifying said greater than 50 different oligonucleotides in said pool of oligonucleotides contacted with said different target nucleic acids to produce modified oligonucleotides;
- e) contacting said modified oligonucleotides with a second substrate comprising probe oligonucleotides, said probe oligonucleotides having sequences different from each other and having sequences different from said pool of oligonucleotides cleaved from said beads, and
- f) detecting said target nucleic acids.

62. (New) The method according to any one of claims 27, 33, 35, or 54 wherein said first substrate comprises greater than 400 different oligonucleotides.

63. (New) The method according to any one of claims 27, 33, 35, or 54, wherein said first substrate comprises greater than 1000 different oligonucleotides.

64. (New) The method according to any one of claims 27, 33, 35, or 54, wherein said first substrate comprises greater than 2000 different oligonucleotides.

65. (New) The method of claim 61, wherein said different beads comprise greater than 400 different oligonucleotides.

66. (New) The method of claim 61, wherein said different beads comprise greater than 1000 different oligonucleotides.

67. (New) The method of claim 61, wherein said different beads comprise greater than 2000 different oligonucleotides.

68. (New) The method of claim any one of claims 27, 33, 35, 54, or 61, wherein said modifying step comprises ligase chain reaction (LCR).

69. (New) The method of claim any one of claims 27, 33, 35, 54, or 61, wherein said modifying step comprises cycling probe technology (CPT).

70. (New) The method of claim any one of claims 27, 33, 35, 54, or 61, wherein said modifying step comprises Invader.

71. (New) The method of claim any one of claims 27, 33, 35, 54, or 61, wherein said modifying step comprises oligonucleotides ligation assay (OLA).

72. (New) The method of claim any one of claims 27, 33, 35, 54, or 61, wherein said modifying step comprises single base extension (SBE).

73. (New) The method of claim any one of claims 27, 33, 35, 54, or 61, wherein said modifying step comprises amplification.

74. (New) The method of claim any one of claims 27, 33, 35, 54, or 61, wherein said modifying step comprises rolling circle amplification.